

Patent Application of

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for

TOPICAL FLUOROQUINOLONE ANTIBIOTICS IN AN ALCOHOL AND ACETONE
VEHICLE

BACKGROUND OF THE INVENTION

This invention relates to the topical application of all fluoroquinolones, including but not limited to, ciprofloxacin, ofloxacin, enoxacin, cinoxacin, pefloxacin, lomefloxacin, norfloxacin, tosufloxacin, fleroxacin, temafloxacin, trovafloxacin, and difloxacin, mixed in an alcohol and acetone vehicle for the treatment of a variety of organisms which infect the skin and a variety of inflammatory skin conditions. It will be in the form of a cream, ointment, lotion, gel, suspension, emulsion, cleansing bar, pledget, salve, tincture, spray, transdermal device, or other appropriate non-toxic pharmaceutical carrier.

Fluoroquinolone antibiotics were first developed in the early 1960s but the earliest one, nalidixic acid, proved particularly susceptible to resistant bacteria thereby making it ineffectual

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over the long term. In the last five years, fluoroquinolones have become increasingly popular as chemical alterations have dramatically decreased the resistant bacteria appearing after treatment. This has made the family of fluoroquinolones more effective than a number of other antibiotics in combating bacterial infections. Fluoroquinolones attack bacteria by targeting DNA gyrase and by interfering with bacterial replication.

These antibiotics have been used extensively to treat respiratory tract infections, urinary tract infections, diarrhea, postoperative-wound infections, and many other conditions, because they are readily absorbed after oral and topical administration and exhibit potent in vitro activity against a broad spectrum of bacterial species. Patent 5,476,854 describes the oral, intravenous and transdermal use of lomefloxacin to treat urinary tract infections, upper respiratory tract infections, sexually-transmitted infections, ophthalmological infections and intestinal infections.

Fluoroquinolone antibiotics are active against a wide spectrum of gram-positive and gram-negative bacteria because of their broad antimicrobial activity. Varieties of fluoroquinolones, specifically ciprofloxacin, have been found to be effective against *Staphylococcus aureus*, *Streptococcus pneumoniae*, coagulase-negative staphylococci, *Streptococcus pyogenes*, *Staphylococcus epidermis*, *Pseudomonas aeruginosa*, *Escherichia coli*, *Klebsiella pneumoniae*, *Enterobacter cloacae*, *Proteus mirabilis*, *Proteus vulgaris*, *Providencia stuartii*, *Morganella morganii*, *Citrobacter diversus*, *Citrobacter freundii*, and other susceptible organisms. The mounting resistance of *Staphylococcus aureus* to both penicillin and erythromycin has made the fluoroquinolone antibiotics a viable alternative for the treatment of

skin diseases. Studies of the effectiveness of the oral treatment of ciprofloxacin on skin and soft tissue infections have shown the medicine to have cure rates of 80% to 100%.

Topical compositions of fluoroquinolones and its derivatives have been used for ophthalmic use, as seen in Patent 4,551,456, which describes the use of norfloxacin and related antibiotics in the topical treatment of ocular infections. Patent 5,374,432 describes a topical composition chosen from aminoglycoside antibiotics and quinolone antibiotics mixed in a sterile carrier, such as a water or ointment base, for the treatment of burns, other infection-prone wounds and ocular infection. Patent 5,401,741 describes the topical treatment of ofloxacin mixed in an aqueous solution, for otopathy.

Combining a fluoroquinolone with a second active ingredient or antibiotic utilizes the two drugs' different mechanisms simultaneously to attack the many varieties of skin infections, inflammations and diseases. Fluoroquinolones have been tested in combination with coumermycin, amikacin, oxacillin, gentamicin, vanomycin, azlocillin, rifampin, and fosfomycin and have shown different degrees of synergy against *Staphylococcus aureus*. Patents 3,944,668 and 4,038,388, combine tetracycline with 8-hydroxyquinoline in a topical or oral application as the two active ingredients behave synergistically against certain micro-organisms. Patent 5,648,389 describes a topical composition mixing an antimicrobial, including ciprofloxacin, with a beta hydroxy acid and water soluble zinc compound to treat acne in humans.

The objective of this invention is to combine all fluoroquinolones, including but not limited to, ciprofloxacin, ofloxacin, enoxacin, cinoxacin, pefloxacin, lomefloxacin, norfloxacin,

tosufloxacin, fleroxacin, temafloxacin, trovafloxacin, and difloxacin, in an alcohol and acetone vehicle for the topical treatment of a variety of skin conditions. The composition will be in the form of a cream, ointment, lotion, gel, suspension, emulsion, cleansing bar, pledget, salve, tincture, spray, transdermal device, or other appropriate non-toxic pharmaceutical carrier.

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DESCRIPTION OF THE INVENTION

While the invention will be described in connection with a preferred embodiment and method, it will be understood that I do not intend to limit the invention to the embodiment or method. On the contrary, I intend to cover all alternatives, modifications, and equivalents as may be included within the spirit and scope of the invention as defined by the appended claims.

In accordance with the present invention, the selected fluoroquinolone antibiotic in combination in an alcohol and acetone vehicle in the form of an ointment, lotion, cream, gel, suspension, emulsion, cleansing bar, pledget, salve, tincture, spray, transdermal device, or other appropriate non-toxic pharmaceutical carrier. As stated above, the resulting composition is used for the topical treatment of a variety of skin infections conditions.

Compositions are prepared by mixing a selected fluoroquinolone antibiotic as an active ingredient with an alcohol and acetone vehicle. In this solution, a fluoroquinolone antibiotic will be added to an independent mixture of acetone, alcohol and water whereby the fluoroquinolone retains its medicinal properties and allows for the topical administration of the antibiotic.

In the following compositions, "Active Ingredient," means any selected fluoroquinolone antibiotic. The respective concentrations of any of the ingredients can vary (0.1% to 99.0%, for example) as different strengths of the composition are produced. The inactive ingredients are representative only and may vary according to need. Various preservatives (such as benzoic acid) will also be added as needed. These preparations describe the manner and processing of

using this invention and are to be construed as exemplary embodiments of the inventive concept and not as limitations thereof.

Example 1

Ointment

	mg/g
Active Ingredient	10.0
Acetone	180.0
SD Alcohol 40	360.0
Mineral Oil	50.0
White Petroleum q.s. ad	1.0

Example 2

Lotion

	mg/g
Active Ingredient	10.0
Acetone	180.0
SD Alcohol 40	360.0
Polyethylene glycol 400	100.0
Hydroxypropyl cellulose	5.0
Propylene glycol q.s. ad	1.0
Purified Water q.s. ad	100.0

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Example 3

Cream

	mg/g
Active Ingredient	10.0
Acetone	180.0
SD Alcohol 40	360.0
Isopropyl myristate	100.0
Polyoxyethylene (2) monostearyl ether	10.0
Polyoxyethylene (20) monostearyl ether	25.0
Propylene glycol	100.0
Purified water q.s. ad	1.0g

Example 4

Gel

	mg/g
Active Ingredient	10.0
Acetone	180.0
SD Alcohol 40	360.0
Hydroxypropyl cellulose	50.0
Allantoin	10.0
Propylene glycol	50.0
Purified water q.s. ad	1.0g


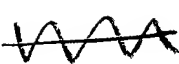
Example 5

Suspension

	mg/g
Active Ingredient	10.0
Acetone	180.0
SD Alcohol 40	360.0
Polyethylene glycol 400	100.0
Hydroxypropyl cellulose	5.0
Propylene glycol q.s. ad	1.0

Example 6

Emulsion



	<u>mg/g</u>
Active Ingredient	10.0
Acetone	180.0
SD Alcohol 40	360.0
Polyethylene glycol 400	100.0
Hydroxypropyl cellulose	5.0
Propylene glycol q.s. ad	1.0

